

EXHIBIT 9

**EXPERT REPORT
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OxyContin in Cancer pain patients, initiated by their Oncologists and then referred back to FPs/GPs/IMs, will result in a comfort level that will enable expansion of use in chronic non-malignant pain patients also seen by the family practice specialists. As we build clinical literature and the FDA becomes more comfortable with our promotion we will be in a position to move our promotion more aggressively into the indications currently reserved for oxycodone combinations and Class III combinations, specifically post-operative pain, musculoskeletal pain, injury/trauma, and CNS pain.⁹⁶

98. A year later, after receiving initial FDA approval for OxyContin, Purdue instructed its sales representatives to aggressively promote OxyContin, noting in a December 17, 1995 OxyContin memorandum that “OxyContin will be the most promoted product in Purdue history.”⁹⁷

99. In my opinion, this aggressive promotion targeted the groups of doctors identified in Purdue’s internal memo, and as explained below, utilized promotional tactics that misbranded OxyContin as a drug that is safer and more effective than it actually is without substantial evidence.

1. Purdue’s Promotion of OxyContin and Opioids in General Minimized the Risks of Abuse, Addiction, Tolerance, and the Effects of Withdrawal.

(a) Purdue’s Marketing Misleadingly Minimized the Similarities Between OxyContin and Morphine.

100. OxyContin is and always has been pharmacologically similar to morphine, including with respect to abuse liability.

100.1. In the NDA for OxyContin, Purdue stated “Oxycodone is an opioid with pharmacologic actions similar to morphine.”

⁹⁶ *Id.*; see also PKY180544129 at 428 (Purdue’s market research anticipated that “a comfort level will be established among FPs [Family Physicians] which could expand to include OxyContin for selected non-cancer pain.”).

⁹⁷ PKY180242947 at 2.

100.2. FDA's Pharmacology Review of the OxyContin NDA concluded that OxyContin is "pharmacologically similar to morphine."⁹⁸

100.3. FDA's Medical Officer Review found that the "distribution of adverse events by body system for CR Oxycodone [OxyContin] is similar to that reported for morphine sulfate."⁹⁹

100.4. The initial OxyContin label stated "OxyContin is a mu-agonist opioid with abuse liability similar to morphine."¹⁰⁰

100.5. The current label for OxyContin contains similar language.¹⁰¹

101. Purdue's pre- and post-approval market research identified a negative "stigma" associated with morphine as to addiction.

101.1. At an OxyContin Investigator's Meeting in June 1995, results from an opioid stigma survey were reported, noting that "among health care providers there is a perception that patients feel a 'stigma' associated with opioid analgesic therapy. Morphine and hydromorphone are most associated with this stigma. One of the patients' biggest fears appears to be the possibility of addiction..."¹⁰²

⁹⁸ PURCHI-000667209 at 140.

⁹⁹ PURCHI-000667209 at 34.

¹⁰⁰ SHC-000006346 at 6. Notably, FDA approved OxyContin for an indication similar to that of Purdue's extended-release morphine product, MS CONTIN. *See id.* at 3 ("OxyContin is intended for the management of moderate to severe pain where use of an opioid analgesic is appropriate for more than a few days.") *compare* MS Contin Label, Jan. 28, 1994, PDD1715073161 at 1 ("[I]ndicated for the relief of moderate to severe pain. It is intended for use in patients who require repeated dosing with potent opioid analgesics over periods of more than a few days."); *see also* MS Contin 1996 PDR at 2.

¹⁰¹ *See* https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022272s040s041lbl.pdf (last visited March 15, 2019).

¹⁰² PKY181823986 at 17; PPLP004030121 at 2; PPLP004030223 at 2; PPLP004030214 at 9; SHC-000004120 at 62.

101.2. This “stigma” was confirmed in focus groups paid for by Purdue and comprised of doctors and nurses in multiple fields, which reported that “there is no question that morphine has a negative stigma with patients relative to both addiction and the terminal nature of their illness.”¹⁰³

101.3. The 1996 OxyContin Formulary Kit copyrighted by Purdue repeated this conclusion, stating “[m]isapprehension concerning the risk of addiction and poor understanding of the concepts of tolerance and physical dependence are part of the problem... Morphine bears a disproportionate share of the stigma associated with opioids, which is intensified by the drug's historic association with terminal disease and helplessness, and with the opium ‘taboo.’”¹⁰⁴

101.4. In a May 28, 1997 email from Purdue’s Michael Friedman to Dr. Richard Sackler, Friedman described the “personality” of OxyContin as being weaker than morphine:

[W]e are well aware of the view, held by many physicians, that oxycodone is weaker than morphine. We all know that this is the result of their association of oxycodone with less serious pain syndromes. This association arises from their extensive experience with and use of oxycodone combinations to treat pain arising from a diverse set of causes, some serious, but most ‘less serious.’ This ‘personality’ of oxycodone is an integral part of the ‘personality’ of OxyContin.”¹⁰⁵

102. The marketing proposals received by Purdue to develop the OxyContin brand recommended utilizing the morphine stigma to gain a competitive advantage for OxyContin.

¹⁰³ PKY181004545 at p. 23; *see also* SHC-000001965 at 2; SHC-000026456 at 46; PKY181004480 at 32; PKY181386644 at 34.

¹⁰⁴ ABT-MDL-KY-0002826 at 11.

¹⁰⁵ PPLP004030150 at 1.

102.1. One advertising agency submitted a proposed brand strategy on April 25, 1994 that highlighted the stigma attached to morphine, asking “how can we capitalize on the perception among patients and physicians that OxyContin does not carry the stigma of morphine through indirect means.” The plan emphasized that one of the “emotional advantages” of OxyContin was that there was “no morphine stigma relating to perception about addiction, tolerance, excessive power, end stage treatment.”¹⁰⁶

102.2. Other advertising agencies similarly proposed brand plans that highlighted the need to differentiate OxyContin from morphine, with one advertising agency recommending that Purdue “separate OxyContin from the ‘addiction’ stigma of morphine-containing products”¹⁰⁷ and another agency noting that the “fear of morphine addiction on the part of patients is a real barrier to treatment of pain. Because of the social issues, people would prefer to take 40 mg of oxycodone rather than 5 mg of morphine.”¹⁰⁸

102.3. In May of 1994, Purdue hired the advertising agency Lavey/Wolff Swift, Inc.,¹⁰⁹ whose proposed brand strategy highlighted that “oxycodone does not carry the stigma or many of the side effects of morphine or other third-step opioids....”¹¹⁰

103. Purdue’s marketing of OxyContin utilized the “stigma” associated with morphine to differentiate OxyContin from morphine, despite their well-known similarities.

¹⁰⁶ PKY180286806 at 11, 13, 38.

¹⁰⁷ PKY180286896 at 39-40.

¹⁰⁸ PKY180287212 at 3.

¹⁰⁹ PKY180250286 at 5.

¹¹⁰ PKY180286723 at 58.

103.1. In the same May 28, 1997 email described above, Friedman explained to Dr. Sackler how Purdue used this “personality” of OxyContin being weaker than morphine in its marketing, writing:

When we launched OxyContin, we intentionally avoided a promotional theme that would link OxyContin to cancer pain. We specifically linked OxyContin to the oxycodone combinations with our “old way, new way” campaign. We made sure that our initial detail piece provided reps with the opportunity to sell the product for a number of different pain states.¹¹¹

103.2. Friedman continued, “it would be extremely dangerous, at this stage in the life of this product, to tamper with this ‘personality,’ to make physicians think the drug is stronger or equal to morphine.”¹¹²

103.3. The following month, on June 22, 1997, Purdue’s Marketing Group Manager for OxyContin, Michael Cullen, reminded the OxyContin product team of the “perception” of OxyContin as weaker than MS Contin and stressed importance of not changing this “perception” in promotional materials:

Since oxycodone is perceived as being a “weaker” opioid than morphine, it has resulted in OxyContin being used much earlier for non-cancer pain. Physicians are positioning this product where Percocet, hydrocodone, and Tylenol with Codeine have been traditionally used.

Since the non-cancer pain market is much greater than the cancer pain market, it is important that we allow this product to be positioned where it currently is in the physician's mind. If we stress the “Power of OxyContin” versus morphine, it may help us in the smaller cancer pain market, but hurt us in the larger potential non-cancer pain market. Some physicians may start positioning this product where morphine is used, and wait until pain is severe before using it.

...

¹¹¹ PPLP004030150 at 1.

¹¹² *Id.*

It is important that we not change the position perception of physicians towards oxycodone when developing promotional pieces, symposia, review articles, etc.¹¹³

103.4. In a June 16, 1997 marketing and sales update, Michael Cullen reminded the OxyContin team that “we can show that we are as ‘effective’ as morphine, but do not want to say OxyContin is as ‘powerful’ as morphine. Words such as ‘powerful’ may make some people think the drug is dangerous and should be reserved for the more severe pain.”¹¹⁴

104. According to Purdue’s marketing team, by differentiating OxyContin from morphine, Purdue was able to expand OxyContin beyond the cancer pain market.

104.1. As noted by Michael Friedman in his email to Dr. Sackler on April 22, 1997, “despite our initial uncertainty, we have been successful beyond our expectations in the non-malignant pain market. Doctors use the drug in non-malignant pain because it is effective and the ‘personality’ of OxyContin is less threatening to them, and their patients, than that of the morphine alternatives.”¹¹⁵

104.2. In another email to Dr. Richard Sackler, Friedman explained that Purdue used this “personality” of OxyContin being weaker than morphine to differentiate OxyContin from MS CONTIN with great success:

Oxycodone has a ‘personality that is influenced by many years of oxycodone use in Percocet. We have built a large part of our platform on this personality and used it to differentiate OxyContin from MS Contin and This differentiation has lead [sic] to much non-malignant business. Marketing is not only about who you are. It is also about what

¹¹³ PPLP004032323 at 4.

¹¹⁴ PPLP004030366 at 1. To that effect, in a sales PowerPoint titled “OxyContin Competitive Market,” Purdue described morphine as “the most potent analgesic” despite OxyContin being more potent than morphine. *See* SHC-000000508 at 37

¹¹⁵ PPLP004030150 at 1.

you are not. We have a success beyond our expectations that is, in part, due to the unique personality of OxyContin.”¹¹⁶

104.3. Years later, on January 25, 2001, Friedman confirmed the success of Purdue’s strategy to distinguish OxyContin from morphine in an email to Mark Alfonso, Purdue’s Executive Director of Marketing, stating that “we were able to convince doctors to use OxyContin tablets because of its position in the doctors mind that is [sic] very different from morphine.”¹¹⁷

105. In my opinion, Purdue’s marketing minimized the similarities between OxyContin and morphine.

(b) Purdue Falsely Marketed OxyContin as Having a Lower Potential for Abuse as Compared to Other Opioid Products

106. Purdue’s early market research also identified the “**biggest negative** of the product [OxyContin] **was the abuse potential**...this was exacerbated by the fact that some felt that Q12h dosing and the lack of APAP or ASA, might make the product more susceptible to addiction.”¹¹⁸

107. To address the reluctance of physicians to prescribe OxyContin for non-cancer pain, market researchers recommended that “Purdue Frederick implement clinicals with OxyContin among non-cancer pain patients to determine if there might be any reductions in side effects that one might get when compared with the combination opioids,” noting that “[i]f the

¹¹⁶ PPLP004030162 at 1.

¹¹⁷ PPLP004030463 at 1.

¹¹⁸ PPLP004031668 at 39. In a December 3, 1996 report titled “OxyContin Research: Self-Administered Questionnaire Among Rheumatologists Prescribers and Non-Prescribers of OxyContin,” which was commissioned by Purdue, it was shown that the most frequently mentioned reason for why a physician would not prescribe OxyContin was “abuse potential (22%).” SHC -000007578 at 3.

product was proven to have a lower abuse potential than IR [immediate release] oxycodone, it would improve the likelihood of usage for non-cancer pain.”¹¹⁹

108. Purdue never conducted a clinical trial specifically evaluating, much less providing substantial evidence, that OxyContin had a lower abuse potential as compared to immediate release oxycodone or any other opioid product.¹²⁰

108.1. In 1993, Purdue conducted a “spoon and shoot” study to determine what constituents could be extracted by grinding OxyContin into a solvent traditionally used by addicts. Purdue and FDA acknowledged the ease in which Oxycodone HCL could be easily extracted in water, “a fact which abusers would most likely learn very quickly.”¹²¹

108.2. Purdue conducted a 4-year registry study, OC97-0302, that evaluated, among other things, instances of drug abuse among patients taking OxyContin.¹²² “Of the 233 subjects who enrolled in OC97-0302, 13 subjects were indicated by the investigators as having signs of ‘drug seeking behavior’ on the case report form.”¹²³ A review by the External Advisory Board (EAB) overseeing the RADARS System (Researched Abuse, Diversion, and Addiction-Related Surveillance System) reduced the number of subjects to 6.¹²⁴ Based on this reduced number, Purdue concluded that “the frequency of ‘drug seeking behavior’ cases that were considered positive or possible for drug abuse or dependence in this study” was no different than the prevalence of drug abuse in the

¹¹⁹ PPLP004031668 at 58. The recommendation by market researchers aligned with the recommendation by FDA that Purdue conduct a long-term OxyContin study of “highly selected” patients with osteoarthritis to examine, among other things, the abuse liability of OxyContin. SHC-000002018 at 1.

¹²⁰ PDD1701345999 at 1-2.

¹²¹ SHC-000007033 at 9.

¹²² See SHC-000007763 at 26

¹²³ See PDD8013445789 at 3223-3224.

¹²⁴ *Id.*

general population based on reports to the National Household Survey on Drug Abuse (NHSDA).¹²⁵

109. In addition, in 1992, 1994, and 1997, Purdue acknowledged that the question of whether OxyContin's extended release design reduced the abuse liability of the drug had not been studied.

109.1. In draft OxyContin labels from 1992 and 1994, Purdue wrote that "parenteral oxycodone has comparable abuse liability to parenteral morphine" and "whether or not the controlled-release dosage form" of OxyContin "would have the same effect is unstudied at present."¹²⁶

109.2. On February 27, 1997, after learning that Purdue was considering selling OxyContin in Germany as an uncontrolled "non-narcotic," which would eliminate the requirement to track instances of abuse, Purdue's then-Vice President of Clinical Research and the inventor of OxyContin, Dr. Robert Kaiko, responded:

b) I don't believe we have a sufficiently strong case to argue that OxyContin has minimal/or no abuse liability:

- in the U.S. oxycodone containing products were once less controlled than now; abuse resulted in greater controls;
- oxycodone containing products are still among the most abused opioids in the U.S.; this information is available to BfArM;
- the local tissue necrosis that can result from injection of OxyContin "fixed" for such abuse is not likely to be a deterrent to abuse; let us not forget that in New Zealand, MST is the most common sources of parenterally abused morphine/heroin;
- **our dossier acknowledges a small handful of patients in our research program who were suspect in terms of their drug accountability;**

¹²⁵ *Id.*

¹²⁶ PDD150109445 at 12; PDD1501101593 at 18. This language was included in the draft package insert submitted by Purdue to FDA as part of the original NDA for OxyContin. See PURCHI-000621046. For reasons unknown at the time of this report, the language appears to have been deleted by FDA during the course labeling negotiations. See PPLPC024000000134; see also PPLP004030136 ("[W]e do not have any abuse liability studies.").

- we do not have a postmarketing abuse monitoring system and data base from which we could conclude that diversion/abuse is not occurring.

c) **If Oxycontin is uncontrolled in Germany, it is highly likely that it will eventually be abused there and then controlled.** This may be more damaging to OxyContin internationally than any temporarily higher sales that would be gleaned from an uncontrolled status; let us not forget the experience with buprenorphine, which was initially uncontrolled: reports of abuse in Germany, in part, eventually led to lots of bad press and controlled status; worldwide sales suffered - even where buprenorphine had been already controlled.¹²⁷

110. Moreover, FDA specifically instructed Purdue not to make claims comparing the OxyContin to other opioid products and rejected any claim of superiority over other opioid products with respect to efficacy and safety. Specifically:

110.1. In the Integrated Summary of Safety (ISS) completed by Dr. Curtis Wright, IV on May 19, 1995 as part of the FDA Medical Officer Review, Dr. Wright stated that “[t]he best conclusion is that the efficacy of [OxyContin] is equivalent to the [immediate-release oxycodone], with an adverse event profile that is as good as the [immediate-release oxycodone]. I would not allow a ‘better’ claim.”¹²⁸

110.2. Dr. Wright also noted in the ISS that “[t]he adverse experience profile of [OxyContin] is qualitatively similar to that of the parent drug, oxycodone;”¹²⁹

110.3. In the FDA Medical Office Review’s Integrated Safety of Efficacy (ISE) completed by Dr. Wright on June 19, 1995, he stated “[t]here is some evidence, both pharmacokinetic and clinical, that reduced acute opioid adverse effects may be expected

¹²⁷ PDD1701345999 at 1-2 (emphasis added).

¹²⁸ PURCHI-000667209 at 37 (original emphasis).

¹²⁹ PURCHI-000667209 at 39.

in some patients, but there is not enough evidence to support an [adverse event] superiority claim [for OxyContin] against other marketed products;”¹³⁰ and

110.4. In the ISE, Dr. Wright also noted that “[c]are should be taken to limit competitive promotion. [OxyContin] has been shown to be as good as current therapy, but has not been shown to have a significant advantage beyond reduction in frequency of dosing.”¹³¹

111. Nonetheless, Purdue’s sales representatives were trained to make misleading statements unsupported by substantial evidence that OxyContin had lower abuse potential as compared to other opioid products, utilizing this statement that was added to the initial label approved for OxyContin: “Delayed absorption, as provided by OxyContin tablets, is believed to reduce the abuse liability of a drug.”¹³²

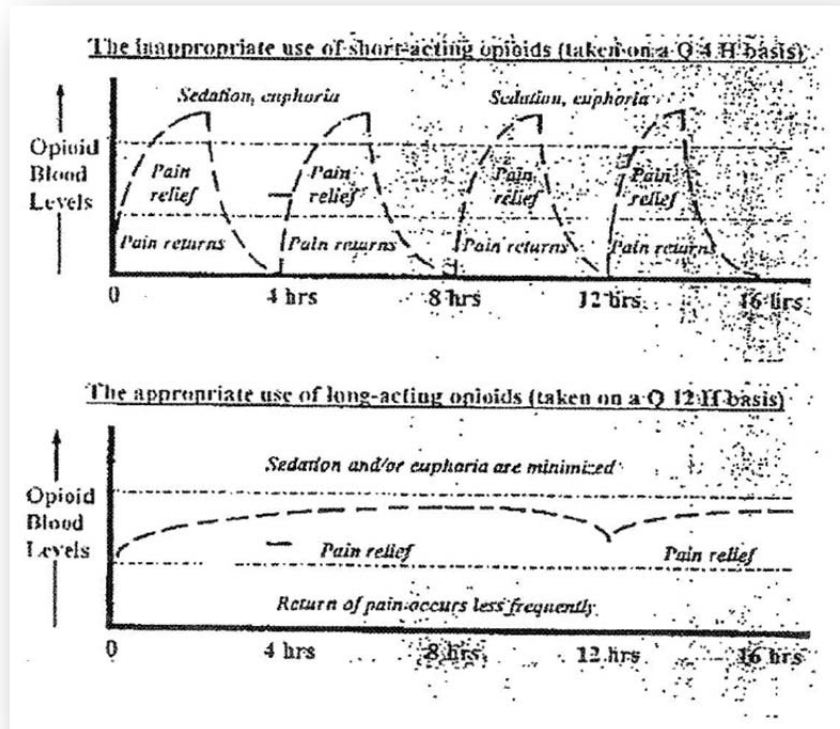
111.1. For example, Purdue held a training session in or about December 1998 for all of its district sales managers where it “falsely stated that OxyContin has significantly fewer ‘peak and trough’ blood level effects than immediate-release opioids resulting in less-euphoria and less potential for abuse than short-acting opioids” and used

¹³⁰ PURCHI-000667209 at 40.

¹³¹ PURCHI--000667209 at 53.

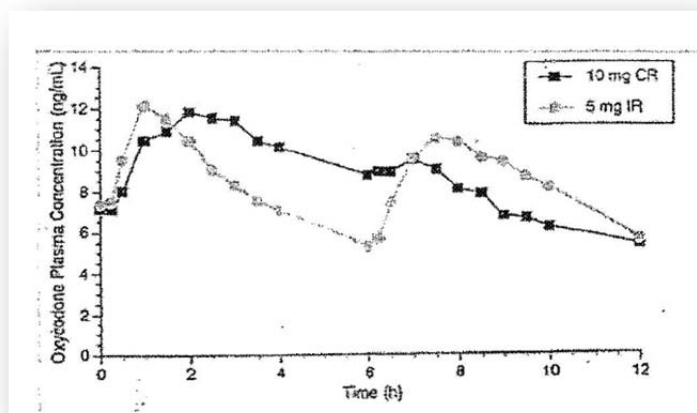
¹³² SHC-000006346 at 6. In response to media reports, Robert Reder, M.D., Purdue’s Vice President, Medical Director has stated that he believes the delayed absorption language was added by FDA. *See* Purdue Pharma Stmt on The Uncertain Hour’s OxyContin episode, December 13, 2017, *available at* <https://www.marketplace.org/2017/12/13/health-care/purdue-statement> (last visited March 15, 2019). This is contradicted by August 2, 1995 handwritten edits to the OxyContin label, which added the delayed absorption language, and were made *after* FDA reviewers submitted their labeling edits to Purdue. *See* SHC-000004520 at 19; *see also* PPLPC02400000133 (circulating FDA edits to OxyContin PI); PPLPC02400000134 (attachment to email). Further, a review of Purdue’s communications log with FDA does not reveal any contact with FDA on or near August 2, 1995 such that FDA directed Dr. Reder to add this language. *See* PPLPC001000135671. In 2001, FDA directed Purdue to remove this language from the label. *See* SHC-000008186. In the deposition of Dr. Curtis Wright, IV, he testified that “I don’t know” who proposed the language “delayed absorption, as provided by OxyContin tablets, is believed to reduce the abuse liability of a drug.” Wright Dep. Tr. 156:16-25, 158:05-14, Dec. 19, 2018. However, Dr. Wright confirmed that the handwritten edits mentioned above were not his. *Id.* at 158:15-159:02.

the following graphical demonstration that was not based on clinical trial data and contravened a prior instruction by FDA to refer to actual data in these demonstrations:



133

¹³³ PDD1712900035 at 8-9; PURCHI-000622957 at 11-12. Below is a graph that accurately portrays the peaks and troughs by blood plasma levels for both OxyContin and immediate release oxycodone, which DDMAC instructed Purdue to use in lieu of the above promotional graphs. PDD1712900035 at 6-7.



111.2. In addition, during training at Purdue's headquarters in or around 1999, "some of PURDUE's new sales representatives were permitted ... to draw their own blood level graphs to falsely represent that OxyContin, unlike immediate-release or short-acting opioids, did not swing up and down between euphoria and pain, and resulted in less abuse potential."

111.3. In handwritten notes from a Purdue sales training that outlined responses to statements from doctors, a sales representative wrote "↑ abuse potential" in response to the statement "I prefer CIII's because I can call them in."¹³⁴

111.4. In undated sales force training materials, Purdue outlined questions to be asked of physicians misleadingly suggesting that OxyContin has low abuse potential:

9. (Using the ladder) "How would you feel about using a drug with:
 - a, the same indication as Vicodin and Ultram on the low end
 - b. with q12h dosing and **low abuse potential**
 - C. as your first pain medication after NSAIDs?

10. (Using the ladder): "How comfortable would you be initiating analgesic therapy after NSAIDS with a dosing regimen more mild than Tylenol #3 dosed q 4h, and **with a low abuse potential?**"

11. (Using the PDB page 24 Figure 7) "Doctor, that's excellent that you are concerned about abuse, that's exactly why the experts are using OxyContin take a look at this graph...**which drug do you think is most likely to lead to abuse potential, the one that dumps all the drug within the first hour causing this spike, or the one the enter the blood stream slowly and smoothly?**"

12. (Using the PDB page 7, last sentence in first paragraph) "Doctor, how do you feel about this statement...do your patients really set their alarm docks at midnight and 4 am? How would you feel if you could prevent this and give the patient pain prevention with **minimum abuse potential?**"

13. "Doctor, Mr. Wil Corbitt, diversion program coordinator for the DEA in the state of Florida, spoke to our group in November 1997. What do you

¹³⁴ SHC-000008102 at 2.

think he said is the biggest street abused drug in Florida? (answer: hydrocodone)...How would you feel about using a pain management tool that, according to the FDA, may have a **reduced abuse potential**?

...

15. "I am worried about my patient becoming dependent on OxyContin (or drugs like it)?" Ask the doctor, "Now do you mean dependent?" Introduce new visual aid and proper definitions Doctor, that's exactly why you should use OxyContin. Show APS page 26 ...risk of iatrogenic addiction is rare show blood levels on page 7 of PDB —Doctor, **which blood level do you think would be more likely to lead to abuse??**

...

26. If there were a pain medication that could provide 96.5% success right after NSAIDs, **with a reduced abuse liability**, how would you feel about using this product? (show package insert or product data brochure validating this success rate)

...

30. Doctor, how would you feel if one pain medication could control moderate pain right after NSAIDs as well as severe pain with a 96.5% success rate and **a reduced abuse potential**?¹³⁵

112. Aligning with the sales training provided by Purdue, Purdue's sales force falsely told health care providers in all fifty states¹³⁶ that the language in the OxyContin label regarding the possibility of reduced abuse potential "meant that OxyContin did not cause a 'buzz' or euphoria, caused less euphoria, had less addiction potential, had less abuse potential, was less likely to be diverted than immediate-release opioids, and could be used to 'weed out' addicts and drug seekers."¹³⁷ For example, Purdue's internal call notes for OxyContin include the following misleading statements by Purdue's sales force:

112.1. May 22, 1996 (Kentucky) - "RETOLD ME THAT CLASS MADE A BIG DIFFERENCE AND **HE FELT THAT HYDORCODONE IS LESS ABUSED, AFTER HEARING THAT IT IS MUCH MORE ABUSED** AND TALKING ABOUT THE ABUSE ISSUES, HE TOLD ME THAT HE WOULD USE IT AND WOULD USE

¹³⁵ SHC-000026573 at 1-4.

¹³⁶ Shapiro Dep. Tr. 235:15-236:01, April 15, 2015, PPLP004030873.

¹³⁷ *Id.* at 210:21-211:12.

IT PREOP. I POINTED OUT THE PI, BUT HE FEELS THAT HE WOULD USE IT PREOP AS WELL AS POSTOP.”¹³⁸

112.2. November 7, 1997 (Ohio) - “ALWAYS RELUCTANT TO USE NARCS BUT TOLD IF GOING TO PUT PT ON VIC/LORT OR TYL 3, WHY NOT USE THE 12 HR DOSED, WITHOUT TYLENOL AND LESS ABUSE POTENTIAL.”¹³⁹

112.3. January 22, 1998 (Ohio) - “THOUGHT OXY WAS JUST FOR CA AND CHRONIC PAIN. TOLD LIKE Q12 HR VIC OR LORTAB/USED FOR ANY TYPE OF PAIN LASTING MORE THAN 4 DAYS.LESS ABUSE POTENTIAL”¹⁴⁰

112.4. May 21, 1998 (Ohio) - “DOES TREAT PAIN/INTERESTED IN-OXY ASKED FOR ANY PTS ON VIC/ORE THAN SEVERAL DAYS. TOLD LESS ABUSE/NO TYLENOL...”¹⁴¹

112.5. August 6, 1998 (Ohio) - “OXY FOR ALL VIC PTS/LESS ABUSE POTENTIAL AND PTS CAN SLEEP THROUGH PM.”¹⁴²

112.6. September 18, 1998 (Ohio) - DR. HAS A TON OF VICO PTS. A LOT OF LOW BACK PAIN. LEARY OF CLASS II'S. USED PI TO SELL LOW ABUSE, Q12H, AND QOFL. DR. AGREED TO USE FOR ALL OF HIS LOW BACK INSTEAD OF VICO. KEEP ON THIS GUY, THIS IS EASY MONEY.¹⁴³

¹³⁸ PPLP004032436 (emphasis added). Call notes are reproduced with minimal, if any, changes to formatting, grammar, spelling, etc., including use of all capital letters. Additional call notes can be found in Schedule 11.

¹³⁹ PKY182139780 (emphasis added).

¹⁴⁰ PKY182139597 (emphasis added).

¹⁴¹ PPLPMDL0030008507 (emphasis added).

¹⁴² PPLPMDL0030008507 (emphasis added).

¹⁴³ PPLPMDL0080000001 (emphasis added).

112.7. July 6, 1999 (Ohio) - “Hit Oxy, **does not like to prescribe narcotics because of abuse and addiction. Turned both objections into adv for Oxy.** Dr liked the fact of low abuse and drastically less tabs.”¹⁴⁴

112.8. July 15, 1999 (Ohio) - Dr. admitted that he has been seeing a ton of drug seekers lately. Has stopped giving oral opioids and will give only an injection. **Hit on low abuse and how pts. would call back screaming if they were given the Oxy in place of the Perco. Dr. agreed.**¹⁴⁵

112.9. September 20, 1999 (Ohio) - “**Dr. thinks that he is going to get busted since he is writting so much Oxy. Reminded him of less tabs and lower abuse.** Discussed using for post op pain esp those chronic painers and how to use as much Oxy to address pts. pain. Discussed tolerance.”¹⁴⁶

112.10. December 18, 2000 (Ohio) - Did get him to admit that **pts. in a LTC would be a good choice for O.C. b/c of low abuse potential** and I shared the Marcus reprint with him.¹⁴⁷

113. Purdue’s sales force likewise falsely told health care providers “that OxyContin has significantly fewer ‘peak and trough’ blood level effects than immediate-release opioids resulting in less-euphoria and less potential for abuse than short-acting opioids.”¹⁴⁸

¹⁴⁴ PPLPMDL0080000001 (emphasis added).

¹⁴⁵ PPLPMDL0080000001 (emphasis added).

¹⁴⁶ PPLPMDL0080000001 (emphasis added).

¹⁴⁷ PPLPMDL0080000001 (emphasis added).

¹⁴⁸ Attach. B to Plea Agreement of *U.S. v. The Purdue Frederick Co. Inc.*, Agreed Statement of Facts, PDD1712900035 at 6.

114. Purdue later stated that “from December 12, 1995 through June 30, 2001, Purdue marketed and promoted OxyContin as ... less subject to abuse and diversion ... than other pain medications.”¹⁴⁹

115. In my opinion, Purdue falsely marketed OxyContin as having a lower potential for abuse as compared to other opioid products.

(c) Purdue Lacked Substantial Evidence Regarding the Addictive Potential of OxyContin, Yet Misleadingly Claimed that OxyContin Was Less Addictive than Competitor Opioid Products.

116. Opioid products, including oxycodone, are addictive.

116.1. The medical literature has recognized the addictive potential of opioids.¹⁵⁰

116.2. The initial OxyContin label warned that OxyContin “may be habit forming.”¹⁵¹

116.3. Purdue acknowledged in 2001 the lack of substantial evidence regarding the rate of addiction, stating “there are no data to accurately characterize the extent of addiction” among patients taking opioids.¹⁵²

¹⁴⁹ *Id.* at 4, 5.

¹⁵⁰ *See, e.g.* Bloomquist. (1963) The Addiction Potential of Oxycodone (Percodan). Reports on Drugs. 99:2; Bouckoms et al. (1992) Chronic Nonmalignant Pain Treated with Long-Term Oral Narcotic Analgesic. Annals of Clinical Psychiatry. 4:3; Fishbain et al. (1992). Drug Abuse, Dependence, and Addiction in Chronic Pain Patients. Clinical J Pain. 8:77-85.

¹⁵¹ *See, e.g.*, SHC-000006346.

¹⁵² SHC-000020630 at 10. Notably, published historical clinical experiences with opioids indicated that iatrogenic addiction was not rare among patients using opioids for prolonged periods of time. *See* Portnow J. (1985). Medically Induced Drug Addiction. Intl J Addict 20:605-611 (“Medically induced drug addiction as a complication of medical treatment is being increasingly recognized as a widespread problem demanding new and innovative solutions.”); Musto D. (1985). Iatrogenic Addiction: the problem, its definition and history. Bull NY Acad Med 61:694-705; Walker L. (1978). Iatrogenic Addiction and Its Treatment. Intl J Addict 13:461-473.

117. From pre-approval market research conducted in 1994 and 1995, Purdue learned that “[t]he medical community is looking for a product that would be efficacious for severe pain, **particularly if it could avoid the . . . addictive potential of the opioids.**”¹⁵³

118. Despite the lack of substantial evidence regarding the addictive potential of opioids and FDA’s instruction not to make claims comparing OxyContin to other opioids,¹⁵⁴ Purdue trained its sales force to tell doctors that the addictive potential of opioids had been greatly exaggerated and that OxyContin was less addictive than competitor opioid products:

118.1. In its 1996 OxyContin launch plan, Purdue stated that “[p]hysicians, nurses and pharmacists are very often resistant to using scheduled drugs in the treatment of pain. This is due to a fear of patient drug addiction.” The plan noted that “[m]ost [physicians] are overly concerned with . . . addiction associated with opioid analgesics.”¹⁵⁵ Hence Purdue asserted in its 1996 Press Release for OxyContin that “[t]he fear of addiction is exaggerated.”¹⁵⁶

118.2. In Purdue’s 1998 marketing “War Book” for OxyContin, Purdue identified key “message points” designed to reinforce OxyContin’s advantage over competitors, one of which included OxyContin’s “low incidence of addiction or tolerance” as compared to competitors.¹⁵⁷

119. Other Purdue promotional materials downplayed the risk of addiction and were targeted at physicians.

¹⁵³ SHC-000026456 at 6 (emphasis added).

¹⁵⁴ See, e.g., PURCHI-000667209 at 36, 40, 53, 94.

¹⁵⁵ PURCHI-003284938 at 1.

¹⁵⁶ SHC-000024730 at 22.

¹⁵⁷ SHC -000004120 at 33.

119.1. On August 4, 1998, Purdue distributed to its entire sales force a sample letter to doctors on addiction. The letter downplayed the risk of addiction, stating “the risk of addiction to opioids in clinical care has been greatly exaggerated” and “[v]ery few patients taking opioids for pain fit this definition,” and instructing doctors to “look at the facts”—specifically, that:¹⁵⁸

[A] survey of more than 11,000 opioid-using patients, taken over several years, found that less than 1% (4 cases) of these patients had documented cases of addiction.

. . .

The risk of opioid abuse or addiction in patients without prior histories of abuse is extremely rare . . .

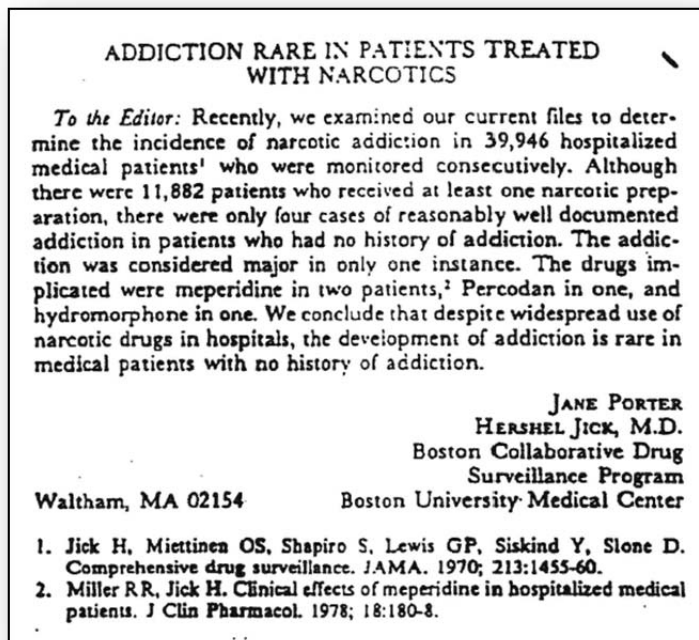
We're confident that effective pain management can be achieved in more patients if physicians like yourself look at the facts. By recognizing the fear of addiction, more and more patients can be helped with opioid therapy.¹⁵⁹

119.2. These “facts” originated from the following five sentence-long letter published by the New England Journal of Medicine in 1980 that provided no information on opioid dose, number of doses, duration of opioid treatment, extent of any long-term follow-up of patients, including whether opioid treatment was continued; or the criteria used to ascertain opioid addiction:¹⁶⁰

¹⁵⁸ PKY180117076 at 11.

¹⁵⁹ *Id.*

¹⁶⁰ Dr. Jick later admitted that he and Dr. Porter submitted the data in letter format to the New England Journal of Medicine because it was not robust enough to merit a study. *See* Barry Meir, *Pain Killer: An Empire of Deceit and the Origin of America's Opioid Epidemic* 33 (2d ed. 2018).



120. Aligning with the sales training provided by Purdue and Purdue's promotional materials, Purdue's sales force misleadingly told health care providers that opioids rarely led to addiction and that OxyContin was subject to less addiction than other opioid products, without substantial evidence:

120.1. November 19, 1997 (West Virginia) - "**CONCERNED ABOUT ADDICTION WITH OPIOIDS**. DIFFERENCE BETWEEN DEPENDENCE AND ADDICTION. **LESS THAN 1% OF PATIENTS BECOME ADDICTED**. CAN ABRUPTLY STOP LOW DOSES OF OXYCONTIN WITHOUT WITHDRAWAL SYMPTOMS"¹⁶¹

¹⁶¹ SHC-000008118 (emphasis added).

120.2. November 21, 1997 (New Jersey) - “HAS AN OPPORTUNITY TO RX PAIN MEDS IN ER AT ST FRANCIS IS CONCERNED WITH ADDICTION BUT AGREES THAT LONG ACTINGS ARE LESS LIKELY TO ADDICT”¹⁶²

120.3. April 23, 1998 (Ohio) - “RPH WAS CONCERNED WITH THE NUMBER OF PATIENTS THAT DR RICHMOND HAS PUT ON OXY, SD THEY ARE ALL PRETTY STRANGE DIS LESS ABUSE AND ADDICTION WITH OXY AND WHY MORE APPROPRMED, DIVERSION RATE OF OXY VS OTHERS”¹⁶³

120.4. May 11, 1998 (Kentucky) - “USE OF FROM START TO WAS UNDER THE IMPRESSION THAT O WAS ONLY THERE TO REPLACE MSC. NOOOOOOO! SHOWED HIM PI INDICATION, PLUS THE NON-ADDICTIVE AND ACET PROBLEM. WHEN I LEFT HE SAID HE WAS SWITCHING THEM ALL OVER TO O FROM HYDROS WE'LL SEE.”¹⁶⁴

120.5. November 4, 1998 (Kentucky) - “BEFORE HAS A WORRY ABOUT THE DEA. TOLD HIM TO TELL THEM, IF ANYTHING EVER HAPPENED, THAT THE PURDUE REP TOLD THEM THAT IT WAS LESS ADDICTING”¹⁶⁵

120.6. March 9, 2001 (Kentucky) - “said speaker for purdue at recent FP mtg said oxy was not addicting.”¹⁶⁶

121. Purdue also created Partners Against Pain, a pain advocacy organization, to promote the claim that addiction to opioids is rare, despite lacking substantial evidence.

¹⁶² SHC-000008111 (emphasis added).

¹⁶³ PKY182142182 (emphasis added).

¹⁶⁴ PPLP004032436 at 80 (emphasis added).

¹⁶⁵ PPLP004032436 at 112 (emphasis added).

¹⁶⁶ PPLP004032436 at 401 (emphasis added).

121.1. For instance, a Partners Against Pain brochure issued in 2000 and titled “Counseling Your Patients and Their Families Regarding The Use of Opioids to Relieve Pain,” stated “a survey of more than 11,000 opioid-using patients, taken over several years, found only four cases of documented addiction” “among patients who regularly take opioids for pain, and have no history of substance abuse...which percentage represents the proportion who become addicted ... 1%.”¹⁶⁷ This brochure cited the Porter & Jick letter.

121.2. In a 2001 “Patient Bill of Rights,” Partners Against Pain stated that “[a]ddiction is very rare in patients without a history of drug/alcohol abuse when taking an opioid under a doctor’s care.”¹⁶⁸

122. Purdue also financially supported, and in some cases controlled, other pain advocacy organizations that put forth promotional materials and engaged in promotional activities that falsely claimed that the risk of opioid addiction had been exaggerated. The following is a brief summary of Purdue’s involvement in these advocacy organization and their false and misleading statements:

122.1. Purdue provided millions of dollars to pain advocacy organizations, including American Pain Foundation, Ameican Pain Society, American Academy of Pain Medicine, the Joint Commission, and the Federation of State Medical Boards.

122.2. These organizations published guidelines and other materials, provided continuing medical education, and otherwise purported to provide “education” to healthcare providers and patients regarding the safe use of opioids.

¹⁶⁷ SHC-000024493 at 11-13.

¹⁶⁸ SHC-000004944 at 5.

122.3. These promotional materials contained statements unsupported by substantial evidence and were therefore false and misleading as to the safe use of opioids, including that the rate of opioid addiction is exaggerated.¹⁶⁹

122.4. Further detail regarding Purdue's involvement in these pain advocacy organizations is provided in Section XI.¹⁷⁰

123. Likewise, Purdue acknowledged in 2007 that it "[t]old PURDUE sales representatives they could tell health care providers that OxyContin potentially creates less chance for addiction than immediate-release opioids."

124. In my opinion, Purdue's marketing misleadingly claimed without substantial evidence that OxyContin was less addictive than competitor opioid products.

(d) Purdue Misleadingly Told Health Care Providers that Patients Exhibiting Signs of Addiction Were Likely "Pseudoaddicted" and in Need of Additional Opioids to Treat Pain

125. Pseudoaddiction is a term to describe a patient who appears "looking like a drug addict" but is instead in pain and displaying symptoms of pseudoaddiction, i.e., "misinterpretation of relief-seeking behaviors as drug-seeking behaviors." It is a term that Purdue's Dr. David Haddox claimed to have coined in 1988.¹⁷¹

¹⁶⁹ See, e.g., PKY180112501 at 11. This brochure, published by Purdue's unbranded organization, Partners Against Pain, repeated Purdue's conclusion that the rate of addiction was less than 1% based on this five-sentence letter, stating "[i]n fact, a survey of more than 11,000 opioid-using patients, taken over several years, found only four cases of documented addiction. ... Many patients—and family members—will be surprised to discover that fewer than 1% of opioid-using patients become addicted!" *Id.*

¹⁷⁰ Attachment B to Plea Agreement of U.S. v. The Purdue Frederick Co. Inc., Agreed Statement of Facts, PDD1712900035 at 6.

¹⁷¹ See PPLP003877027 at 9; Weissman, D. and J. Haddox. (1989). Opioid pseudoaddiction--an iatrogenic syndrome. *Pain*. 36(3): 363-66.

126. Pseudoaddiction is not supported by substantial evidence. In 2009, the American Pain Society and the American Academy of Pain Medicine, two pain advocacy organizations supported by Purdue, reviewed the claim of pseudoaddiction, finding:

We identified no systematic reviews or primary studies on accuracy of tools for differentiating drug-related behaviors due to inadequate symptom relief from true aberrant drug-related behaviors. The few studies that evaluated drug-related behaviors due to inadequate symptom relief in patients with chronic noncancer pain have not attempted to validate criteria for diagnosing this condition.¹⁷²

127. Prior to this, these and other pain advocacy organizations supported by Purdue published “educational” materials that recognized pseudoaddiction as a medical condition despite the lack of substantial evidence.¹⁷³

128. Often utilizing the materials published by these pain advocacy organizations, Purdue’s sales force promoted pseudoaddiction when physicians reported addicted patients or otherwise raised concerns about addiction to OxyContin.¹⁷⁴

128.1. April 9, 1998 (Ohio) - TALKED 3 APPROACH TO MOVING PAT OFF
OF S ACTING REM AND TOLER ACROCONT AND NO PROB WITH PH IE
ACID/ALKALINE SAME RELEASE EACH TIME. MUST TALK OXY KEYSARE
MORE PREDICTLEVELS VS ... AND REMIND HS DOSING AND PH INDEPEND
DELIV **SHOW HIM PSEUDO ADDICT AND NEED TO DOSE UP TO PAIN**
LEVEL SUGG FOR 6 PERCS LOOK AT RANGE AND INC DOSE ONE NOTCH¹⁷⁵

¹⁷² ENDO-OPIOID_MDL-01463855 at 102.

¹⁷³ See Section XI.

¹⁷⁴ A Purdue regional sales manager testified that a sales representative, when faced with a physician concerned about prescribing a higher dose of OxyContin because of addiction, should suggest the dose be adjusted upwards since the patient may be pseudoaddicted. Chris Sposato Dep. Tr. 145:5-147:19, Jan. 22, 2003, PDD9520404001.

¹⁷⁵ PPLPMDL0080000001 (emphasis added).

128.2. August 14, 1998 (Ohio) - F/U ON PHN PAT ON T3 3/DAY GO WITH 10-20 Q12H USING 10S **LOOK AT HIS CONCERNS DEA/ADDICTION REVIEW PSEUDOADDICT** SHOW MELNICK AND BROCHURE STRESS QOL AND PAT BENEFITS GOOD NIGHT REST ASK FOR 1 PAT GO AFTER OSTEO NEXT¹⁷⁶

128.3. November 2, 1998 (Ohio) - CONT TO ASK FOR OXY TO BE USED FOR NEW STARTS SHOW PKGE INSERT LESS ABUSE/SHOW BLOOD LEVELS PREDICT STRESS BEST PAIN MED ON MKT MOST PREDICT **ASK TO SWITCH PSEUDO ADDICTS TO OXY** WANTRING EARLY REFILLS CLOSE FORE THESE PAT¹⁷⁷

128.4. June 21, 1999 (Ohio) - **OXY ADDICTION VS PSEUDO**, DISEASE STATE MGT AND TITRATION ISSUES COPD AND UNI VS BID THEO¹⁷⁸

128.5. February 17, 2000 (Ohio) - obj: to find out what type pain patients she is treating with oxy Action: she is treating failed back patients for the most part she actually mentioned no longer treating patients with opioid therapy because she keeps getting dinged by patients seeking **we discussed pseudoaddiction vs addiction** as well as the OSMA book on pain and the 5th Vital Sign I left her with an opioid documentation kit-she is not sure her mind will be changed I mentioned if she is going to choose to use an opioid, oxy is the safest one to use¹⁷⁹

128.6. November 29, 2000 (Ohio) - he is so hungry for information-went over the comfort assessment journal and empowering hispatients to take more control of their

¹⁷⁶ PPLPMDL0080000001 (emphasis added).

¹⁷⁷ PPLPMDL0080000001 (emphasis added).

¹⁷⁸ PPLPMDL0080000001 (emphasis added).

¹⁷⁹ PPLPMDL0080000001 (emphasis added).

situation-as well as how hwe is assessinf **talked pseudo addiction physocological dependence** and proper titratiom of oxycontin gave his Coles Ten tips¹⁸⁰

128.7. December 1, 2000 (Ohio) - discussed one of his patients that he dismissed from the practice because of abuse-**we discussed the source of her pain and pseudo addiction as well as psychological dependence**-¹⁸¹

128.8. October 28, 2002 (Ohio) - issues here today as doing inservice are patients coming to them asking for oxycontin and **he feels they are selling it for \$80 / day** or more and just too tempting asked him what drug can he write that this can't occur **disc**... **pseudo addiction** and conntracts witih patient she feels better now...¹⁸²

128.9. October 17, 2003 (Ohio) - Gave Barrett and Marsa Columbus invite. Barrett pointed out Rush story. **Reminded him that under tx can = pseudo addiction and that if not good pain doc it can and will happen**. Marsa very rushed, but says he is using as 1st choice for po long acting.....¹⁸³

129. Purdue also created the pain advocacy organization, Partners Against Pain, which promoted pseudoaddictoin, among other claims about opioids.

129.1. In 2001, Partners Against Pain provided the following definition of pseudoaddiction in a "Pain Management Kit" that was distributed to healthcare providers: "Pseudoaddiction is a term which has been used to describe patient behaviors that may occur when pain is undertreated. Patients with unrelieved pain may become focused on obtaining medications, may 'clock watch,' and may otherwise seem inappropriately 'drug

¹⁸⁰ PPLPMDL0080000001 (emphasis added).

¹⁸¹ PPLPMDL0080000001 (emphasis added).

¹⁸² PPLPMDL0080000001 (emphasis added).

¹⁸³ PPLPMDL0080000001 (emphasis added).

seeking.’ Even such behaviors as illicit drug use and deception can occur in the patient’s efforts to obtain relief.”¹⁸⁴ Partners Against Pain repeated this definition in the 2005 and 2007 versions of its “Pain Management Kit.”¹⁸⁵

129.2. In a Partners Against Pain 2007 “Defining Key Terms in Pain Management” document, the following definition was provided for pseudoaddiction: “Pseudoaddiction is a term which has been used to describe patient behaviors that may occur when pain is undertreated. Patients with unrelieved pain may become focused on obtaining medications, may ‘clock watch,’ and may otherwise seem inappropriately ‘drug seeking.’ Even such behaviors as illicit drug use and deception can occur in the patient’s efforts to obtain relief.”¹⁸⁶

129.3. In its 2009 Pain Management Kit, Partners Against Pain stated that the following were “behaviors [are] less suggestive of an addiction disorder,” including “aggressive complaining about the need for more drug;” “drug hoarding during periods of reduced symptoms;” “requesting specific drugs;” “opening acquiring similar drugs from other medical sources;” and “unsanctioned dose escalation...”¹⁸⁷

130. Purdue likewise supported other pain advocacy organizations to make similar misleading claims about pseudoaddiction.¹⁸⁸

¹⁸⁴ PPLP003326602 at 56.

¹⁸⁵ PPLP004114967 at 4; PPLP003341378 at 1.

¹⁸⁶ PPLP003326602 at 56.

¹⁸⁷ PKY181695113 at 53.

¹⁸⁸ See Section XI.

131. In addition, Purdue's key opinion leaders were instructed on pseudoaddiction,¹⁸⁹ and gave presentations and otherwise conveyed the concept of pseudoaddiction to healthcare providers despite lacking substantial evidence to support the claim.¹⁹⁰

132. In my opinion, Purdue misleadingly told health care providers that patients exhibiting signs of addiction were likely "psuedoaddicted" and in need of additional opioids to treat pain.

(e) Purdue Minimized the Risks of Tolerance and Physical Dependence that Patients Could Experience with OxyContin

133. Known side effects of OxyContin include "tolerance" and "physical dependence."¹⁹¹

134. "Tolerance" is "the need for increasing doses of opioids to maintain a defined effect such as analgesia," and "physical dependence" is "the occurrence of withdrawal symptoms after abrupt discontinuation of a drug."¹⁹²

135. Both conditions "are not unusual during chronic opioid therapy."¹⁹³

136. Despite this, Purdue downplayed their risks in OxyContin promotional materials provided to health care providers. For instance, Purdue's sales representatives distributed reprints of a December 1998 article published by Robert Reder, MD, Purdue Vice President and Medical Director, and Sanford Roth, MD, a rheumatologist and speaker¹⁹⁴ for Purdue, which discussed the

¹⁸⁹ PDD1503981005 at 75.

¹⁹⁰ PDD1502210202 at 827 (identifying the speaker training presentation as "accredited continuing education").

¹⁹¹ SHC-000006346 at 4.

¹⁹² *Id.* see also Phillips JK, Ford MA, Bonnie RJ. (2017). Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use. National Academies Press, *available at*: <https://www.ncbi.nlm.nih.gov/books/NBK458661/Phillips>.

¹⁹³ SHC-000006346 at 4 (emphasis added).

¹⁹⁴ See E513_00004803 at 9 (identifying Dr. Sanford as a speaker for a Purdue sponsored event); SHC-000024908 at 19 (identifying Dr. Sanford as a speaker at a Purdue symposium/luncheon).

“misconceptions” of opioids, including that “tolerance is rarely a practical problem in opioid therapy.”¹⁹⁵

137. Likewise, in promotional materials from 1996 through at least 2008, Purdue did not prominently disclose the possibility of tolerance or physical dependence to OxyContin.¹⁹⁶ Instead, Purdue focused primarily on the benefits of OxyContin.

137.1. For example, in or around December of 1996, Purdue sent to healthcare providers the following letter failed to present a fair and balanced evaluation of the risks and benefits of OxyContin by failing to disclose the possibility of tolerance or physical dependence to OxyContin:

On your formulary, q12h OxyContin can enhance pain control, because it provides:

- The analgesic efficacy of oxycodone* with the ease of q12h dosing
- Twelve hours of smooth and reliable pain control—less frequent dosing than with Percocet, Vicodin, or Tylenol with Codeine
- Analgesic onset within 1 hour in most patients
- Single-entity therapy—no aspirin or acetaminophen which may be potentially toxic in maximal daily doses
- No “ceiling” to analgesic efficacy—may be titrated upward when clinically necessary
- Diminishing side effects (except constipation) over time for many patients

OxyContin is a logical “next step” when around-the-clock (A-T-C) opioid therapy is needed. We are confident it is a logical “next choice” for your formulary.¹⁹⁷

¹⁹⁵ Sanford R. (1998). The Role of Opioids in the Treatment of Osteoarthritis. Resident & Staff Physician. 44(12):21-36, PDD1701869808.

¹⁹⁶ See, e.g., PURCHI-000550536; PURCHI-000723096; PURCHI-000723253; PURCHI-000723352; PURCHI-000723681; PURCHI-000723829; PURCHI-000723966; PURCHI-000724367; PURCHI-000763440; PURCHI-000813598; PURCHI-000830011

¹⁹⁷ PURCHI-000723253 at 70.

137.2. Similarly, the following September 18, 2003 promotional material used by Purdue as a display at a healthcare convention failed to present a fair balance of information relating to risks and benefits in that it did not prominently disclose the risks of tolerance and physical dependence to OxyContin.¹⁹⁸

For moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time

THERE CAN BE LIFE WITH RELIEF

- **Q12h dosing convenience**
- **Onset of analgesia within 1 hour in most patients***
- **Convenient conversion and titration**
- **OxyContin® is an opioid agonist and a Schedule II controlled substance with an abuse liability similar to morphine. Consider this when an increased risk of misuse, abuse, or diversion is a concern**
- **OxyContin® Tablets are NOT intended for use as a prn analgesic**
- **OxyContin® TABLETS ARE TO BE SWALLOWED WHOLE AND ARE NOT TO BE BROKEN, CHEWED, OR CRUSHED. TAKING BROKEN, CHEWED, OR CRUSHED OxyContin® TABLETS LEADS TO RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF OXYCODONE**
- **OxyContin® 80 mg and 160 mg Tablets ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY.** These tablets may cause fatal respiratory depression when administered to opioid-naïve patients
- The most serious risk with OxyContin® is respiratory depression, which can be fatal
- OxyContin® is not indicated for pre-emptive analgesia, pain in the immediate postoperative period (the first 12 to 24 hours following surgery) in patients not previously taking OxyContin® (because its safety in this setting has not been established), or pain that is mild or not expected to persist for an extended period of time
- As used here, "moderate" and "moderate to severe" pain do not include commonplace and ordinary aches and pains, pulled muscles, cramps, sprains, or similar discomfort

* From a single-dose study.
Reference: 1. Sunshine A, Olson NZ, Colon A, et al. Analgesic efficacy of controlled-release oxycodone in postoperative pain. J Clin Pharmacol. 1996;36:595-603.

Q12h
OXYCONTIN® II
(OXYCODONE HCl CONTROLLED-RELEASE) TABLETS
IT WORKS

Please read professional prescribing information, including boxed warning, available at this exhibit.

Copyright 2003, Purdue Pharma L.P., Stamford, CT 06901-3431 AP090-F1 PUR-4001195A

138. Purdue's pain advocacy organization, Partners Against Pain, also made statements that discussed the ability to increase the dose of opioids without adequately addressing the significant risk of doing so.¹⁹⁹

¹⁹⁸ PURCHI-000723966 at 19.

¹⁹⁹ Purdue also supported pain advocacy organizations that downplayed these risks. See Section XI.

138.1. A 2005 brochure titled “Clinical Issues in Opioid Prescribing” stated “[i]f opioid doses are gradually increased, high dosages are generally well tolerated and not associated with respiratory depression” without discussion of physical tolerance or dependence.²⁰⁰

138.2. Similarly, in the 2000 brochure titled “Counseling Your Patients and Their Families Regarding The Use of Opioids to Relieve Pain,” Partners Against Pain stated the following without discussing the associated risks with opioids “[u]nlike nonopioid pain relievers, an opioid has no ‘maximum’ daily dose-which allows us to adjust the dose to an effective level, no matter how severe your pain” and “[r]emember, opioids are not limited to a ‘maximum’ dose as nonopioids are-an effective dose can be found for virtually any type or severity of pain.”²⁰¹

139. Even when Purdue acknowledged the risks of physical dependence in marketing OxyContin, Purdue downplayed their clinical significance. Specifically, Purdue minimized the severity of withdrawals symptoms resulting from physical dependence,²⁰² which per the OxyContin label, included restlessness, lachrymation, rhinorrhea, yawning, perspiration, chills, myalgia and mydriasis, among others.

139.1. In Purdue’s 1996 sales training, Purdue stated that tolerance and physical dependence do not pose a major clinical problems and that “it is usually not difficult to withdraw an opioid when it is no longer required,”²⁰³ which Purdue’s sales force conveyed to healthcare providers.

²⁰⁰ PPLP004114967 at 6.

²⁰¹ SHC-000024493 at 7, 9

²⁰² Purdue also supported pain advocacy organizations that downplayed these risks. See Section XI.

²⁰³ ABT-MDL-KY-0008846 at 63-64.

139.2. Purdue downplayed physical dependence and its associated withdrawal symptoms at a Purdue dinner symposium at the May 1997 convention of the National Association of Orthopedic Nurses. There, according to a summary provided by a Purdue sales representative, Elizabeth Narcessian, MD, “an active member of Purdue’s Speaker’s Bureau” who helped train other speakers as well as Purdue sales representatives,²⁰⁴ provided the following information to the 510 nurses in attendance about withdrawing from OxyContin:

Dr. Narcessian used an analogy that seemed to get across the addiction vs physical dependence issue. She said that if you drink coffee regularly and stop drinking it one morning, you will most likely get a headache (a withdrawal symptom). That is physical dependence, similar to the withdrawal effect experienced when an opioid is stopped.²⁰⁵

140. Purdue also misleadingly told healthcare providers without substantial evidence that “withdrawal symptoms” from physical dependence would not occur at lower doses but “when high dose opioid therapy is suddenly stopped,”²⁰⁶ such as at doses of 60 mg/day or higher.²⁰⁷

141. Since 1999, and possibly earlier, Purdue was aware reports of withdrawal symptoms in patients stopping OxyContin at doses less than 60 mg per day, and in as early as March 28, 2001, Purdue was aware of concerns regarding the accuracy of the withdrawal data in its published osteoarthritic study.

²⁰⁴ SHC-000024908 at 12.

²⁰⁵ PKY180254414 at 3.

²⁰⁶ Sanford R. (1998). The Role of Opioids in the Treatment of Osteoarthritis. Resident & Staff Physician. 44(12):21-36, PURCHI-000816988 at 21; *see also* Exhibit B to Plea Agreement of *U.S. v. The Purdue Frederick Co. Inc.*, Agreed Statement of Facts, at 9-13.

²⁰⁷ *Id.*; *see also* Sanford R. et al. (2000). Around-the-Clock, Controlled-Release Oxycodone Therapy for Osteoarthritis-Related Pain. Arch Intern Med. 160:853-860, PPLP003983624 at 7; *see also* Gasdia Dep. Tr. 248:16-22, June 27, 2008.

141.1. Purdue learned through a long-term clinical study evaluating OxyContin in osteoarthritis patients (Clinical Study OC92-1103) that physical dependence (and associated withdrawal symptoms) occur even at low doses. In this study, case report forms documented that 13 patients experienced symptoms of withdrawal during periods in which patients were instructed not to take OxyContin. Of the 13 patients, 3 withdrew during the respite period and were taking OxyContin doses less than 60 mg per day. Of the remaining 10 patients, all but two were taking doses lower than 60 mg per day.²⁰⁸ Purdue did not include these as instances of withdrawal in its final study report for OC92-1103, which it submitted to FDA on January 16, 1997.²⁰⁹

141.2. Approximately two years later, on February 12, 1999, an affiliate of Purdue²¹⁰ conducted a meta-analysis of the long-term clinical studies available for OxyContin, which included OC92-1103 and another Purdue clinical study, OC92-1101. This meta-analysis likewise identified instances of withdrawal in patients taking less than OxyContin 60 mg per day.²¹¹

141.3. After the issuance of this meta-analysis by a Purdue affiliate, Purdue—along with Dr. Sanford Roth and other clinical investigators—published the study results of OC92-1103 in a medical journal. In this published study, Purdue reported only two instances of withdrawal following abrupt cessation of doses of 60 mg/day or higher,

²⁰⁸ PPLPC024000037828 at 1-2 (identifying 3 subject who discontinued during respite because of adverse experiences due to possible withdrawal symptoms and additional 10 unique subjects who experienced adverse experiences due to possible withdrawal symptoms).

²⁰⁹ PURCHI-000566584.

²¹⁰ PKY180803001 at 8 (“Purdue Pharma LP, the US associate of Napp Pharmaceuticals Ltd.”).

²¹¹ *Id.* at 35-39.

which according to Purdue, “indicat[ed] that CR oxycodone at doses below 60 mg/d can be discontinued without tapering the dose if the patient's condition so warrants.”²¹²

141.4. Purdue utilized this published study to understate the risk of physical dependency and withdrawal; specifically:

On or about June 26, 2000, certain PURDUE supervisors and employees sent the full text of the osteoarthritis study article together with a “marketing tip” to PURDUE’s entire sales force. The marketing tip stated that a reprint of the osteoarthritis study article was available for use in achieving sales success. The marketing tip also included as one of the article's twelve key points: “There were 2 reports of withdrawal symptoms after patients abruptly stopped taking CR oxycodone at doses of 60 or 70 mg/d. Withdrawal syndrome was not reported as an adverse event during scheduled respites indicating that CR oxycodone at doses below 60 mg/d can be discontinued without tapering the dose if the patient condition so warrants.”²¹³

141.5. Purdue did not take affirmative action to correct this inaccurate information and continued to distribute reprints of the article to sales representatives, who in turn, distributed the false and misleading information to healthcare providers.²¹⁴

142. In my opinion, Purdue minimized the risks of tolerance and physical dependence that patients could experience with OxyContin.

(f) Purdue’s Marketing Minimized the Risks of Respiratory Depression, Addiction, and Abuse Associated with Higher Doses of OxyContin

143. From early market research, Purdue learned that physicians were concerned with prescribing opioid combination products, i.e., opioids combined with aspirin or acetaminophen

²¹² Roth S. et al. (2000). Around-the-Clock, Controlled-Release Oxycodone Therapy for Osteoarthritis-Related Pain. Arch Intern Med. 160:853-860, PPLP003983624 at 7.

²¹³ Attach. B to Plea Agreement of *U.S. v. The Purdue Frederick Co. Inc.*, Agreed Statement of Facts, PDD1712900035 at 12.

²¹⁴ *Id.* at 12-13.

such as Vicodin or Percocet, because “the toxicity limitation of the combination drugs ... precluded their use for the most severe pain, since it was not possible to give enough medicine to control the pain without putting the patient in danger.”²¹⁵ This “danger” was the concern of renal or hepatic toxicity from excess doses of aspirin or acetaminophen.

144. Purdue recognized that OxyContin, as a single-opioid agent, would not have this dose-limiting property, and in Purdue’s early market research, physicians identified “the absence of toxicity concerns as currently exist with the combination products” as an “important strength” of OxyContin and found “no dose ceiling” to be a “strong copy point” in which to market OxyContin.²¹⁶

145. Purdue highlighted this point in its promotion of OxyContin, telling physicians, for example, that “[a]s a single-entity opioid with no ceiling to analgesic efficacy, OXYCONTIN Tablets may be used at doses not limited by maximum permitted doses of NSAIDs or acetaminophen in fixed-combination products.”²¹⁷

²¹⁵ PKY181386644 at 27.

²¹⁶ *Id.* at 31, 34.

²¹⁷ PURCHI-00072320 at 24; *see also* PURCHI-00072310 at 13 (“Doses of opioid agonists such as oxycodone have no ceiling effect for analgesic activity, as evident in the wide dosage range of OXYCONTIN Tablets used in long-term clinical trials.”); *Id.* at 24 (“As a single-entity opioid with no ceiling to analgesic efficacy, OXYCONTIN Tablets may be used at doses not limited by maximum permitted doses of NSAIDs or acetaminophen in fixed-combination products.”); PURCHI-00072310 at 48 (“No ceiling to analgesic efficacy. With full agonists, such as oxycodone ‘effectiveness with increasing doses is not limited by a ‘ceiling.’ OxyContin may be dosed upward as clinically necessary.”); PURCHI-00072310 at 58 (“OxyContin has no ‘ceiling’ to its analgesic efficacy and may be titrated upward, when clinically necessary, with confidence.” (emphasis added)); PURCHI-000550536 at 38 (“Not limited by analgesic ‘ceiling’ or maximum daily dose. OxyContin may be dosed as high as clinically necessary.”); PURCHI-000672849 at 20 (“OxyContin may be titrated as high as clinically necessary, unlike analgesic products such as Percocet, Vicodin, Lorcet, Darvocet-N, and Tylenol with Codeine, or their generic equivalents. OxyContin can be titrated upwards every 24-48 hours, when clinically necessary, until an effective dose is reached, with acceptable side effects.”); PDD9316729260 at 67 (“There is added dosing flexibility with a single agent, since a variety of co-analgesics and adjuvant medications can be used to enhance the individual patient’s pain relief, while having the freedom to dose OxyContin Tablets as high as is clinically necessary.”); PURCHI-000701440 at 9 (“Consider the daily limitations. Many short-acting opioids contain a nonopioid analgesic that limits the maximum daily dose. OxyContin is a single-entity agent that does not contain acetaminophen, aspirin or ibuprofen. Ceiling to analgesic effectiveness is limited only by side effects.”).

146. In doing so, however, Purdue did not balance the significant risks associated with taking larger doses of OxyContin—namely, the potentially fatal risk of respiratory depression²¹⁸ and the increased risk of abuse.²¹⁹

147. Specifically, in marketing OxyContin, Purdue’s sales representatives emphasized that OxyContin has no dose ceiling, encouraging healthcare providers to increase the dose of OxyContin without discussing the risks associated with dose increases.

147.1. February 2, 1996 (Ohio) - BRIEFLY DISCUSSED OXY AND UNIMENTION. DISCUSSED WHO STEP APPROACH AND USE IN STEP 2 WITH OXYCODONE. AND ALSO USE IN NON MALIGNANT PAIN WITH LOWER ABUSE POTENTIAL. **STRESSED Q12H DOSING WITH OXY AND NO DOSE CEILING.** FOLLOW ON 2/12 WITH MORE DETAIL FROM PI ON OXY. FIND OUT WHERE HE SEES IT FITTING IN.²²⁰

²¹⁸ SHC-000006346 at 3; *see also* Phillips JK, Ford MA, Bonnie RJ. (2017). Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use. National Academies Press, *available at*: <https://www.ncbi.nlm.nih.gov/books/NBK458661/Phillips>.

²¹⁹ *See* Dunn, K.M., et al., Opioid prescriptions for chronic pain and overdose: a cohort study. *Ann Intern Med*, 2010. 152(2): p. 85-92; Gomes, T., et al., Opioid dose and drug-related mortality in patients with nonmalignant pain. *Arch Intern Med*, 2011. 171(7): p. 686-91; Bohnert, A.S., et al., Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA*, 2011. 305(13): p. 1315-21; Paulozzi, L.J., et al., A History of Being Prescribed Controlled Substances and Risk of Drug Overdose Death. *Pain Med*, 2012. 13(1): p. 87-95; Zedler, B., et al., Risk Factors for Serious Prescription Opioid-Related Toxicity or Overdose among Veterans Health Administration Patients. *Pain Med*, 2014; Bohnert, A.S., et al., A Detailed Exploration Into the Association of Prescribed Opioid Dosage and Overdose Deaths Among Patients With Chronic Pain. *Med Care*, 2016. 54(5): p. 435-41; Dasgupta, N., et al., Cohort Study of the Impact of High-Dose Opioid Analgesics on Overdose Mortality. *Pain Med*, 2016. 17(1): p. 85-98; Bohnert, A., et al., Understanding Links among Opioid Use, Overdose, and Suicide. *N. Engl. J. Med* 2019; 380:71-9. In addition, Purdue acknowledged in 2001 that “[t]olerance to opioids which results in a dosage increase” was a “side effect” contributing to the abuse of OxyContin and that “[p]atients would therefore benefit from the reduction of the development of tolerance ...” (emphasis added).

²²⁰ PPLPMDL0080000001 (emphasis added).

147.2. March 6, 1997 (Ohio) - LIKES OXY BECAUSE OF FEWER SIDE EFFECTS. **STRESSED NO CEILING AND 80MG.** WILL SEND LIVE W/L²²¹

147.3. January 8, 1998 (Ohio) - USING OXY FOR OSTEO AL;SO STATING WITH PHN/DN **KEEP REM TO INC DOSE NO CEILING** REMIND QOL ADV AFTER NSAID UNIPH SHOW MARTIN TELL HIM CONVERS IS RIGHT TO DOSHOW QD BETTER THAN BIDID.²²²

147.4. January 20, 1999 (Ohio) - **MUST CONT TO STRESS ADV AND ABIL TO INC DOSE NO CEILING** WANTS A 60 MG DOSE SAID HAS MANY ON 20S/40S SUGG EITHER INTERVAL DOSING WITH 40S OR SWITCH TO 80MG Q12H²²³

147.5. February 9, 1999 (Ohio) - HE IS GOOD ON DOSING **HAS NOT EXCEEDED 80 Q12H YET CONTIN TO STRESS NO CEILING BUT SEEMS TO BE COMING AROUND ON THIS ISSUE** STILL FEELS TOLER IS SEEN BETWEEN 40-80 MG MUST....²²⁴

147.6. January 28, 2000 (Ohio) - MD ALWAYS SEES ME CARRYING IN SAMPLES OF SENOKOT WHICH STARTS CONVERSATION; MD SEEMS TO BE TRULEY THANKFUL FOR THE SAMPLES THAT HE RECEIVES; **OXY DISCUSSED RE: NO CEILING DOSE AND EASE OF TITRATION;** OXY

²²¹ PPLPMDL0080000001 (emphasis added).

²²² PPLPMDL0080000001 (emphasis added).

²²³ PPLPMDL0080000001 (emphasis added).

²²⁴ PPLPMDL0080000001 (emphasis added).

IR/FAST FOR BREAKTHROUGH PAIN; CONVERSION CHARTS LEFT WITH MD FOR HIS REVIEW.²²⁵

147.7. February 23, 2000 (Ohio) - Titration call again, went over no ceiling and that 80mg is far from too much. Dr said he gets the message and said he has used the 80mg.²²⁶

147.8. July 6, 2000 (Ohio) - SPOKE WITH MD WHO EXPRESSED CONCERN RE: ONE PT RECEIVING 120 MG Q 12 FOR BACK PAIN- DISCUSSED THE PFACT THAT THERE IS NO CEILING DOSE WITH OXY LIKE SHORT ACTING; HE SEEMED TO THINK THAT THIS PT WAS ABUSING THE PRODUCT; HE NEEDS REAFFIRMATION RE: THE DECREASED ABILITY OF OXY TO BE ABUSED AND DECREASING NUMBER OF TABS....²²⁷

147.9. August 11, 2000 (Ohio) - asked r to to upgrae to the 80 mg q 12 h for difficult pat - dr. agrees - positioned oxy ir for breakthrough reminder detail to dr. on oxy - stay w message - push the high dose - sampled uni and senokot reminded dr that 160 mg tab is coming out - he asked abt oxy fast for break - does not have in southside - y-town - disc high dose pat - 40 mg q 12 h asked if he would write oxy ins of ... for diff pat - disc the inconsist of pain control w ... - asked if he would write 80mg oxy instead of ... - said he will write more oxy f reminded dr that oxy has no ceiling - that he can go above 80 mg - also the potency of oxy vs vic is =n asked dr what he does after 40 mg q 12 - he adds ... - explained the no ceiling of oxy - told him 60 -80mg q 12 is a low dose

²²⁵ PPLPMDL0080000001 (emphasis added).

²²⁶ PPLPMDL0080000001 (emphasis added).

²²⁷ PPLPMDL0080000001 (emphasis added).

of a med that has no limits - says he will go up in dose before switching - was surprised to learn that oxy is no ceiling compared to combos - asked many q about hospice pat and nurses - wanted to know what chevlen does - lots of oxy - 1--1.5 ratio less hal and naus - fu on dosing up and acute vs vic.²²⁸

147.10. January 19, 2001 (Ohio) - doc said he has been using oxy for awhile and that he uses high doses, **i reminded doc there is no ceiling and that he should not worry about how high he needs to go.**²²⁹

147.11. April 6, 2001 (Ohio) - OK w Oxy has (post op back) pt on 80mgs q 12h with Oxy IR q4 in between, talked about titrating up to 100mgs q12 h, at first said he was going to refer to Dr Chevlen, **thinks something else may be going on afraid of higher doses- told of no ceiling**, pt is coming in next week, hopefully he will give this a try before referral. Invited to Dr G's RT but staff doubtful if he will attend because he frequently works until 7:00pm.²³⁰

147.12. March 20, 2003 (Ohio) - Spoke with Dr in clinic, **Dr asked me about a max dose with OxyContin. I went over the idea of no ceiling with any single entity drug and that what actually limits combos is acet and apap.** I explained the advantage of being able to titrate to effect with out worry of acet or apap toxicity.²³¹

148. According to depositions of Purdue employees, Purdue generated greater revenue off the higher doses of OxyContin,²³² and Purdue encouraged its sales force to promote higher

²²⁸ PPLPMDL0080000001 (emphasis added).

²²⁹ PPLPMDL0080000001 (emphasis added).

²³⁰ PPLPMDL0080000001 (emphasis added).

²³¹ PPLPMDL0080000001 (emphasis added).

²³² Sposato Dep. 18:21-24, PDD9520404001.

doses of OxyContin by utilizing a unique incentive system that bonused sales representatives based on increasing dollar volume of sales and not on the number of prescriptions written as is the usual practice.

148.1. As explained by Karen White, a sales representative for Purdue from 1998 to 2002, bonusing on the increase in dollar sales meant “[i]t would exponentially affect our bonuses. I mean if we got the doctor, as I mentioned earlier, to write an 80 milligram instead of a 10 milligram, we would make seven and a half times more money based on what percentage of our sales that we increased over our quota.”²³³

148.2. As a result of this incentive structure, according to Ms. White deposition testimony, sales representatives were encouraged to call on pill mills:

[T]he other reason that I have a problem with [the incentive structure] it is that it behooved us to call on what I refer to as pill mill doctor, doctors who are inappropriately prescribing narcotics. If a Purdue representative knew from one source or another that a doctor was inappropriately prescribing and was a pill mill, a lot of times they didn't turn them in to Purdue because they were making tons of money off of these doctors prescribing OxyContin in the place of other medications. And they were typically prescribing high doses of OxyContin in a lot of cases.²³⁴

148.3. Ms. White's testimony is further supported by a 2001 internal sales memo in which Purdue highlighted to sales representatives that they should “[f]ocus on high prescribers ~ 2-4 calls per month.”²³⁵

149. In my opinion, Purdue's marketing minimized the risks of respiratory depression, addiction, and abuse associated with higher doses of OxyContin.

²³³ White Dep. 98:23-99:14, Dec. 17, 2003, PKY182895039; *see also* Sposato Dep. 18:21-19:2, PDD9520404001. (“Q. My question is: Same amount of pills, higher dosage, Purdue makes more money for the higher dosage, correct? A. That's correct. Q. And that factors into someone's bonus, correct? A. Possibly.”).

²³⁴ White Dep. 99:15-25, PKY182895039.

²³⁵ ABT-MDL-KY-0050021 at 5.

2. Endo Promoted Opana ER in a Manner that Understated Its Risks and Overstated Its Benefits.⁴²⁵

(a) Endo Falsely Marketed Opana ER as Having a Lower Abuse Potential and as Safer than Other Opioid Products

218. Oxymorphone, the opioid molecule in Opana ER, has a history of abuse that can be traced back to the 1960s when it was sold by Endo in immediate release form under the trade name Numorphan.⁴²⁶

218.1. In a May 2011 Drug Intelligence Brief, the DEA's Philadelphia Division Intelligence Program described Numporphan as a popular opioid of abuse.

In the early 1970s, oxymorphone in the form of Numorphan instant-release tablets was one of the most sought-after and well-regarded opioids of the class IV drug using community. Popularly known as 'blues' for their blue coloring, the tablets contained very few insoluble ingredients—making them extremely easy to inject—and they were dangerously potent when used intravenously. 'Blues' were also considered to be especially euphoric; better than heroine or morphine."⁴²⁷

218.2. Similarly, the National Institute on Drug Abuse ("NIDA") reported in 1974 that "Numorphan (oxymorphone immediate release) . . . was found to be the object of increased abuse since its appearance in 1966." NIDA cited Numorphan's "rapid onset of action and prolonged duration of effect" as reasons for its popularity.⁴²⁸

219. Endo has likewise acknowledged that Opana ER has an abuse liability similar to other opioids.

⁴²⁵ Kristin Vitanza, Endo's Brand Manager for Opana ER, testified on behalf of Endo that all "Endo reviewed and approved [] promotional materials for . . . Opana ER, both original and reformulated . . ." "were . . . made available for use nationwide in the promotion of Opana ER." Kristin Vitanza Depo Tr. 282:11-283:3.

⁴²⁶ Numorphan was approved for sale in the U.S. in 1959. ENDO-OPIOID-MDL-00156028 at 3.

⁴²⁷ ENDO-OR-CID-00694804 at 2; *see also* WATKINS, TORRINGTON D. & CARL D. CHAMBER, DRUG ABUSE: CURRENT CONCEPTS AND RESEARCH, 307-09 (KEUP, WOLFRAM, ED., 1972) (As of 1972 "abuse of Numorphan appear[ed] to be rather widespread geographically" with "Numorphan . . . identified by its various subcultural names—numorphine, blue morphine, blue morphan, or blues . . .").

⁴²⁸ Endo's predecessor, Endo Laboratories, withdrew Numorphan immediate-release tablets from the market in 1979. ENDO-OPIOID-MDL-00156028 at 3.

219.1. The label for Opana ER warned of Opana ER's abuse liability in a prominent, Blackbox warning reserved for serious or life-threatening risks, noting an abuse liability similar to other opioids:

WARNING: Opana ER contains oxymorphone, which is a morphine-like opioid agonist and a Schedule II controlled substance, *with an abuse liability similar to other opioid analgesics*. Oxymorphone can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing OPANA ER in situations where the physician or pharmacist is concerned about an increased risk of . . . abuse . . .⁴²⁹

219.2. In addition, Endo's Abuse Liability Assessment for Oxymorphone Extended Release Tablets described the "Risks" of the drug as including that "Oxymorphone is an opioid agonist and a Schedule II controlled substance. It is expected to have an abuse liability similar to other strong opioid analgesics, such as morphine and oxycodone."⁴³⁰

219.3. Endo also included abuse of Opana ER as one of the risks addressed in the Risk Minimization Action Plan ("RiskMAP") for Opana ER,⁴³¹ stating "[t]he goals and objectives for this RiskMAP are to minimize the following liabilities with opioid class of drugs as it pertains to Opana ER . . . Aberrant behavior such as . . . drug abuse . . . [a]mong patients" and "[i]n the community, particularly among your adults." Robert

⁴²⁹ 2006 Opana ER Label (Emphasis in original and added). The current label for Opana ER contains a Blackbox warning with similar language regarding the abuse liability of the drug. *See* 2016 Opana ER Label (ENDO-OPIOID_MDL-00046776 at 4) ("Opana ER exposes users to risks of addiction, abuse, and misuse, which can lead to overdose and death.")

⁴³⁰ ENDO-OPIOID_MDL-00235234 at 36. Abuse of oxymorphone can be traced back to the 1970s. In 1974, the National Institute on Drug Abuse stated in "Drugs and Addict Lifestyles," that "Numorphan (oxymorphone immediate release) . . . was found to be the object of increased abuse since its appearance in 1966. Reasons for its popularity seem to be that it provides rapid onset of action and prolonged duration of effect." FERGUSON, PATRICIA ED., DRUGS AND ADDICT LIFESTYLES, NATIONAL INSTITUTE ON DRUG ABUSE RESEARCH, 237 (1974). In 1979, Endo withdrew Numorphan immediate-release tablets from the market. EPI000130489 at 8.

⁴³¹ EPI000750019 at 8.

Barto Dep. Tr. 1/30/2019 140:7-13, 21-141:7, 142:20-143:2 (“Endo worked with FDA to establish these goals and objectives, and these were the agreed-to goals and objectives with FDA as part of this RiskMAP.”)

219.4. Recently, on January 10, 2019, Endo’s former vice president of sales, Larry Romaine, likewise testified that Opana ER does not have “low abuse potential.”⁴³²

220. Endo witnesses testified that Endo was not permitted to market Opana ER as having less abuse.

220.1. Endo’s former Chief Compliance Officer, Colleen Craven, testified during her deposition, “I agree that Endo was not allowed to say that there was less abuse,” or “less possible diversions of Opana ER for any reason.”⁴³³

220.2. Similarly and in response to the question “you agree that Endo was not allowed to make any of these statements in this sentence about Opana ER: Less abuse, less possible diversion; cannot be crushed; none of the statements were allowed to be made, right?” Ms. Craven testified: “Correct.”⁴³⁴

220.3. Endo’s Vice President of Sales and Regional Business Director, Ronald Jackson similarly testified that it would be “improper” for Endo sales reps “to try to downplay stated risks with respect to a product.”⁴³⁵

221. Despite testimony from Endo’s witnesses that it was not permitted to market Opana ER as having less abuse liability, Endo’s sales force falsely marketed Opana ER as safer than other opioids because of reduced abuse liability.

⁴³² See, e.g., Larry Romaine Depo. Tr. 352:12-14, 16-24.

⁴³³ Collen Craven Dep. Tr. (356:13-357:3, 357:5-7).

⁴³⁴ Craven Dep. Tr. (358:1-6).

⁴³⁵ Ronald Jackson Depo. Tr. 289:9-12.

221.1. Following the launch of Opana ER in June 2006, Endo commissioned market research to identify physician perceptions of Opana ER called Awareness, Trial and Usage (“ATU”) studies.⁴³⁶ These studies confirmed that Endo’s messages that Opana ER had low abuse potential and was safer were being delivered to physicians.

221.2. A June 2007 ATU study of physician recall/perceptions reported that “low abuse potential and safety and tolerability were regarded as the main advantage of Opana ER.”⁴³⁷

221.3. A 2008 ATU study confirmed that one year later physician perceptions remained similar. The study stated that physician awareness of Opana’s “lack of street value” led to “a perception of lower potential for street abuse.”⁴³⁸ The study also reported that physicians who anticipated prescribing increases for Opana ER over the next 6 months” cited “‘low abuse potential’” as one of two major reasons for choosing Opana ER.⁴³⁹

221.4. Market research from 2008 indicated that “PCPs prefer hearing that the agent they select for treatment would be less risky and therefore, easier for them; they reported a sense of calm after reading the ‘simple’ statement.”⁴⁴⁰

221.5. In an Opana ER W2 IVR Vocal Response Listing examining Endo sales representative in-person sales presentations, certain doctors reported that the “main message of the most recent presentation [they] received” for Opana ER included “Less

⁴³⁶ *Id.* at 342:18-343:4.

⁴³⁷ *Id.* at 343:8-12, 343:16-344:2, 5-6.

⁴³⁸ ENDO-CHI_LIT-00547543 at 12.

⁴³⁹ *Id.*

⁴⁴⁰ ENDO-CHI_LIT-00023299 at 38.

euphoria and maybe less addictive potential,” “safe, long acting, *less abuse potential*,” and “The delivery system and *low abuse potential*.”⁴⁴¹

221.6. A December 2008 ATU Final Report stated that Opana ER had “an opportunity to build on one of its most important strengths—low abuse potential.”⁴⁴²

221.7. Endo’s market research from 2008 showed that “Low abuse Potential” was the primary factor influencing physicians’ anticipated increase in use of Opana ER.”⁴⁴³

221.8. Endo sales reps facilitated letters written by doctors to the West Virginia Medicaid Pharmaceutical & Therapeutics Committee, that understated the risk of abuse, stating “Opana ER has a unique delivery system which involves a Matrix, thus allowing it to be given twice a day. The Matrix also allows for the chance of less abuse and possible diversion since it cannot be crushed allowing for injection or nasal administration.”⁴⁴⁴

221.9. In 2009 and 2010, between 15- 21% of physicians surveyed maintained the perception that “advantages of Opana ER” included “low abuse potential.”⁴⁴⁵

221.10. Endo’s Vice President of Sales, Larry Romaine, testified that “Endo could have sent out a Dear Doctor letter to the prescribers it was servicing,” in order to correct the misperception that Opana ER had a low abuse potential and that this

⁴⁴¹ ENDO-CHI_-LIT-00150080 (Emphasis added).

⁴⁴² ENDO-CHI_LIT-00547543 at 17.

⁴⁴³ ENDO-CHI_LIT-00023299 at 59.

⁴⁴⁴ ENDO-OPIOID_MDL-0380727 at 3.

⁴⁴⁵ ENDO-CHI_LIT-00023394 at 55; ENDO-CHI_LIT-00012061 at 37. Six percent of physicians interviewed reported that “[l]ow abuse potential” was the “first thing that comes to mind when [they] think of Opana ER.” *Id.* at 36.

misperception was driving their prescription decisions.⁴⁴⁶ Mr. Romaine could not recall whether such a letter was sent.

222. In my opinion, Endo falsely marketed Opana ER as having a lower abuse potential and as safer than other opioid products.

(b) Endo Minimized the Risk of Addiction Associated with Opana ER and Funded Various Pain Organizations to Likewise Minimize the Risk of Addiction

223. Oxymorphone is known to be addictive, which Endo recognized in seeking approval of Opana ER.

223.1. An article from the New England of Journal of Medicine included in the Opana ER NDA explained: “[t]here can be no doubt, however, that prolonged administration of Numorphan [oxymorphone] represents considerable addiction liability.”⁴⁴⁷

223.2. Addiction risk as it pertains to Opana ER was also one of the risks that Endo told FDA it was addressing through its Risk Minimization Action Plan (“Risk Map”) for Opana ER.⁴⁴⁸

224. Nonetheless, Endo minimized the addiction potential of oxymorphone discussed above by telling healthcare providers and patients that the risk of addiction with Opana ER and opioids was low.

⁴⁴⁶ Larry Romaine Dep. Tr. 360:9-12, 16-21, 360:24-361:14.

⁴⁴⁷ ENDO-OPIOID-MDL-00235351 at 4.

⁴⁴⁸ EPI000750019 at 8 (“The goals and objectives for this RiskMAP are to minimize the following liabilities with opioid class of drugs as it pertains to Opana ER . . . Aberrant behavior such as . . . addiction . . . [a]mong patients” and “[i]n the community, particularly among your adults.”); Robert Barto Dep. Tr. 1/30/2019 140:7-13, 21-141:7, 142:20-143:2 (“Endo worked with FDA to establish these goals and objectives, and these were the agreed-to goals and objectives with FDA as part of this RiskMAP.”)

224.1. A 2009 Opana ER “Instant Savings” card and Resource Kit promising patients up to \$300 in savings asked “What is the risk of becoming addicted to a long-acting opioid?” In response, the accompanying information kit stated “[m]ost healthcare providers who treat patients with pain agree that patients treated with prolonged opioid medicines usually do not become addicted.”⁴⁴⁹

224.2. Endo’s website for Opana, www. Opana.com broadcasted the statement “Most doctors who treat patients with pain agree that patients treated with prolonged opioids medicines usually do not become addicted” until at least 2012.⁴⁵⁰

225. Endo also delivered the misleading message that opioids have low addiction potential through pain advocacy organizations and medical societies it funded.⁴⁵¹

225.1. A December 2007 NIPC *Pain Management Today* newsletter told healthcare providers: “[p]atients are also concerned with being looked upon as ‘druggies’ even though risk of addiction in the general population treated with chronic opioid therapy is extremely low. This adds to the psychological issues that often accompany chronic pain conditions.”⁴⁵²

⁴⁴⁹ ENDO-CHI_LIT-00541205 at 7. A 2010 Oxymorphone Franchise Tactical Plan by Chad Simon, Sr. Product Manager, for the OPANA Brand, reported that the Opana Instant Savings Program had a 14% redemption rate in 2009 for a total of 58,227 redemptions in the range of \$21-25 nationally and between 4,000 and 7,000 redemptions in Ohio. ENDO-CHI_LIT-00039111 at 31.

⁴⁵⁰ END00474717 at 23.

⁴⁵¹ According to Endo’s May 2012 response to the Hon. Max Baucus and Hon. Charles E. Greeley, then Chairman and a member of the Senate Finance Committee, between 1997 and 2012, Endo paid millions of dollars to the American Pain Foundation, American Academy of Pain Medicine, American Pain Society, American Geriatrics Society, University of Wisconsin, Beth Israel Medical Center, the Joint Commission on Accreditation, and the Federal State Medical Boards. ENDO-OR-CID-00754369 at 24-32.

⁴⁵² KP360_OHIOMDL_000027041; Ms. Kitlinski testified that it was Endo’s “intent” “that doctors of all backgrounds, of all specialties, in training or in practice for a long time, had exposure to the company’s supported education programs,” including through the NIPC.” Linda Kitlinski Dep. Tr. (1/15/2019) 395:11-19, 395: 22-24, 396:1-7.

225.2. Endo also provided financial assistance to the American Academy of Pain Medicine (“AAPM”) and the American Pain Society (“APS”), and distributed to healthcare providers the 1997 AAPM/APS consensus statement, which downplayed the risk of addiction, stating that “studies indicate that the de novo development of addiction when opioids are used for the relief of pain is low.”⁴⁵³ The Consensus Statement failed to identify any of the “studies” that it claimed “indicate[d] that the de novo development of addiction when opioids are used for the relief of pain is low.”⁴⁵⁴

226. In my opinion, Endo minimized the risk of addiction associated with Opana ER and funded various pain organizations to likewise minimize the risk of addiction.

(c) Endo Falsely Told Healthcare Providers that Patients Exhibiting Signs of Addiction Could be Exhibiting “Pseudoaddiction” and in Need of Additional Opioids to Treat Pain

227. As described in the Purdue section, the concept of pseudoaddiction is not supported by substantial evidence.

228. Despite a lack of substantial evidence for the concept of pseudoaddiction, Endo included the term in its sales training materials for Opana ER.

228.1. A 2006 Endo sales training document entitled “Module 3: Oxymorphone Risk Management Program” contained a list of definitions “of five important but commonly misunderstood terms” including “Pseudoaddiction,” which it defined as a “term used to describe iatrogenic phenomenon in which a patient with undertreated pain

⁴⁵³ ENDO-OPIOID_MDL-00925807. Endo distributed the Consensus Statement including as part of its risk minimization plan for generic oxycontin and Opana ER. EPI000799695 at 14; ENDO-OPIOID_MDL-01500831 at 14.

⁴⁵⁴ The Consensus Statement was prepared by “committee members” and a “consultant,” many of whom were paid speakers for Purdue, e.g., J. David Haddox, *see* PKY180955294, *see* _____, Russell K. Portenoy, MD, *see* PKY180357269.

is perceived by healthcare professionals to exhibit behaviors similar to those seen in addiction but is not truly addicted.”⁴⁵⁵

228.2. The sales training document added: the “physician can differentiate addiction from pseudoaddiction by speaking to the patient about his/her pain and increasing the patient’s opioid dose to increase pain relief. Pseudoaddiction behaviors such as clock watching (counting down the time until the next dose) will resolve when the pain is properly treated.”⁴⁵⁶

229. In addition, pain advocacy and professional medical organizations supported by Endo published “educational” materials that recognized pseudoaddiction as a medical condition despite the lack of substantial evidence.⁴⁵⁷ For example, at a 2009 NIPC CME on Chronic Opioid Therapy: Understanding Risk While Minimizing Analgesia, Dr. Perry Fine, a paid speaker,⁴⁵⁸ discussed a hypothetical patient who although instructed not to change her pain treatment plan without consulting her doctor, increased her short-acting opioid. Dr. Fine told an audience of healthcare providers:

We need to understand the definitions of pseudoaddiction and behaviors that may resemble frank abuse or addictive behaviors which, in fact, may be extinguished by good pain control. It is a very important distinction to make.” “The diagnosis is extraordinarily important since addiction is a primary neurobiological disease that is life threatening and needs to be very carefully managed, where pseudoaddiction may reflect a very different issue.” Dr. Fine concluded “In view of this differential diagnosis, Dr. Jones believes that in fact this may represent a combination of tolerance and pseudoaddiction and behaviors that are motivated by pain rather than drug-seeking, per se.”⁴⁵⁹

⁴⁵⁵ ENDO-CHI_LIT-00053284 at 15.

⁴⁵⁶ *Id.* at 16. The sales training module cited to the “AAPM, 2001” for these statements. *Id.*

⁴⁵⁷ *See* Section XI.

⁴⁵⁸ *See, e.g.*, KP360_OHIOMDL_000037538.

⁴⁵⁹ KP360_OHIOMDL_000121559 at 1, 26.

229.1. Pseudoaddiction was also taught to 3rd and 4th year residents and fellows in Anesthesiology, Neurology, Family Practice, Emergency Medicine and Physical and Rehabilitation Medicine at the APS's Endo-supported "Fundamentals of Pain Management" "intensive two-day course" attended by more than 1,150 residents and fellows.⁴⁶⁰ Specifically, a slide in the 2009 syllabus for the APS's "Fundamentals of Pain Management" stated: "Differential Diagnosis of Aberrant Drug-Taking Attitudes and Behavior" and included "Pseudoaddiction (inadequate analgesia)" as one of five diagnoses along with addiction, chemical copers, other psychiatric diagnosis, and criminal intent."⁴⁶¹

229.2. As late as 2012 NIPC continued to deliver a message of pseudoaddiction to healthcare providers. An NIPC Dinner Dialogue CME entitled Responsible Opioid Prescribing in the Era of REMS,⁴⁶² attended by 486 prescribers from around the country⁴⁶³ including Columbus, Ohio,⁴⁶⁴ presented a clinical case and asked "Although NB had good general pain control with use of his treatment plan, over time, his pain has increased, and he has increased his dosage of medication without permission with no additional benefit. What is the differential diagnosis? 1. Tolerance, 2. Pseudoaddiction, 3. Addiction, 4. Misuse, 5. Abuse, 6. Diversion."⁴⁶⁵

⁴⁶⁰ Linda Kitlinski Deposition, Ex. 41.

⁴⁶¹ ENDO-OPIOID_MDL-05968029 at 38.

⁴⁶² CHI-000929476 at 1.

⁴⁶³ KP360_OHIOMDL_000336756 at 1.

⁴⁶⁴ KP360_OHIOMDL_000336605 at 2.

⁴⁶⁵ ENDO-OR-CID-01252970 at 57; *see also id.* at 58 (pseudoaddiction is defined as "syndrome resulting from undertreatment of pain that is misidentified by the clinician as inappropriate drug-seeking behavior. Behavior ceases when adequate pain relief is provided. Not a diagnosis; rather, a description of a clinical interaction.")

230. In my opinion, Endo falsely told healthcare providers that patients exhibiting signs of addiction could be exhibiting “pseudoaddiction” and in need of additional opioids to treat pain.

(d) Endo’s Promotion of Opana ER Minimized the Risks of Respiratory Depression, Addiction and Abuse Associated With Higher Doses

231. Consistent with Purdue’s minimization of the risks associated with higher doses of opioids in its message that OxyContin had no dose ceiling, Endo told healthcare providers that the dose of Opana ER could be adjusted upward without disclosing the potentially fatal risks of respiratory depression and the increased risk of abuse.

231.1. A 2009 Opana ER “Instant Savings” card and Resource Kit told potential Opana ER patients “[s]ome people taking opioids may need to take a higher dose after a period of time in order to have relief from their pain. This is ‘tolerance’ to opioid medications that doesn’t affect everyone who takes them and does **NOT** mean addiction. (Emphasis in original). If tolerance develops, it does not mean you will ‘run out’ of pain relief. Your healthcare provider can adjust your dose or prescribe another medicine.”⁴⁶⁶

231.2. An Endo sponsored brochure entitled Understanding Your Pain: Taking Oral Opioid Analgesics brochure delivered a similar message regarding opioids. In response to the question, “what should I know about opioids and addiction,” the brochure stated: “If tolerance does occur, it does not mean you will ‘run out of’ pain relief. Your dose can be adjusted or another medicine can be prescribed.”⁴⁶⁷

⁴⁶⁶ *Id.*

⁴⁶⁷ ENDO-CHI_LIT-00237187 at 3.

232. In my opinion, Endo's promotion of Opana ER as having no dose ceiling misleadingly minimized the risks of respiratory depression, addiction and abuse associated with higher doses.

(e) Endo Overstated the Benefits of Opana ER With Respect to Work and Functionality

233. Endo did not have adequate and well controlled clinical studies demonstrating that Opana ER improved functionality.

234. Nevertheless, Endo promoted Opana ER as providing pain relief that increases patients' functionality.

234.1. A "Clinical Case Study" featuring a clinical perspective by Gerald M. Aronoff, MD presented a hypothetical patient overview of "Laurie."⁴⁶⁸ Under "Patient Assessment/Diagnosis," it stated "Laurie is an otherwise healthy middle-aged woman presenting with inadequately controlled chronic back pain despite total daily dose of 120 mg OxyContin plus oxycodone/acetaminophen 5 mg/325 mg PRN for supplemental rescue medication. Patient reports difficulty remaining active because of her chronic pain, resulting in a sense of loneliness and isolation."⁴⁶⁹ The "Treatment Goals and Plan" section of the case study stated "[t]he ultimate goal of therapy will be to obtain an appropriate balance between management of pain and suffering, improving daily function, and minimizing opioid-related adverse actions . . . Help Laurie, who may feel isolated and stranded due to her condition, by developing a comprehensive pain management plan . . . Begin OPANA ER (oxymorphone HCl) Extended-Release tablets,

⁴⁶⁸ ENDO-CHI_LIT-00138534 at 3.

⁴⁶⁹ *Id.*

CII, with INTAC technology plus supplemental rescue therapy with OPANA Immediate Release (IR).⁴⁷⁰

234.2. Endo also used hypothetical patient profiles to tout the functionality benefits of Opana ER. In a 2007 “Bill the Patient” profile used with physicians, Endo presented Bill—a “40 year old male construction worker who needs to work to support his family,” with “moderate to severe low back pain treated with pain medication for several months,” and whose “[p]hysician has determined patient is appropriate for continuous around-the-clock opioid therapy.”⁴⁷¹

234.3. In a 2011 patient profile, Endo presented “Frank,” an “[a]uto mechanic whose job requires him to stand on his feet all day,” and who has “been treated for chronic low back pain for 3 years.” The promotional piece continued “[b]ecause Frank is not experiencing adequate pain relief, his physician has been upwardly titrating his dose to increased side effects . . . Frank needs a different long-acting opioid.”⁴⁷²

235. In my opinion, Endo misleadingly overstated the benefits of Opana ER with respect to work and functionality.

3. Endo’s Risk Minimization Action Plan for Opana ER Contained Elements that Understated the Risk Abuse and Addiction and Misleadingly Claimed that Patients Exhibiting Signs of Addiction Were Likely “Pseudoaddicted”

236. To address the risks posed by Opana ER, prior to approval, on October 4, 2001, FDA informed Endo that a risk management program for the drug would be needed at the time of approval.⁴⁷³

⁴⁷⁰ *Id.* at 4.

⁴⁷¹ ENDO-CHI_LIT-00033952.

⁴⁷² ENDO-CHI_LIT-00099937 at 1.

⁴⁷³ ENDO-OPIOID_MDL-00159347 at 4.

and complete corrective messaging about the violations discussed above to the audiences that received the violative promotion is warranted.

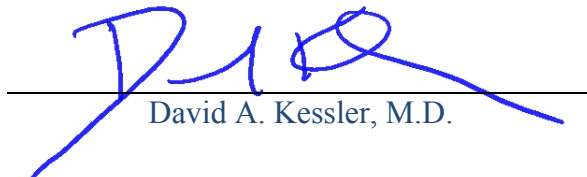
51. In my opinion, the need for corrective promotion here is supported by research that has demonstrated that similar corrective promotion can be effective in countering false and misleading statements made about prescription drug products.

52. In my opinion, manufacturers should assure that no claims, including any superiority claims, about opioids are made without validation of those claims by high quality and well controlled clinical studies.

53. In my opinion, to correct the results of past practices, manufacturers should not fund treatment guidelines, organizations that issue treatment guidelines, or any authors of guidelines that concern pain, opioids or addiction. Disclosure of past and present funding from manufacturers to organizations and individuals that issue or author treatment guidelines should also be made.

54. Based on the totality of the above, it is my opinion that the manufacturers' departures from FDA standards would be expected to (and likely did) have an affect on how healthcare providers prescribed opioids, contributing to a shift in the practice of medicine with regards to the use of opioids in the treatment of pain. This change in the practice of medicine led to an increase in opioid prescriptions, an increase of opioids in interstate commerce, and an increase in inappropriate use of opioids, all of which in turn increased the risk of opioid abuse and contributed to a public health crisis.

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